Compositions Comprising Biomimetic Proteoglycan Constructs; Early, Minimally Invasive Intervention

Primary Investigator

Michele Marcolongo, PhD, Drosdick Endowed Dean, College of Engineering

Background and Unmet Need

Despite decades of research and development into potential disease-modifying Osteoarthritis (OA) drugs (DMOADs), none have been approved for use in humans, partly due to inadequate drug delivery to target joint tissues. A significant obstacle to successful drug intervention is poor pharmacokinetics.[1] As drugs are rapidly cleared (hours to days) from the joint cavity following intraarticular injection, many struggle to penetrate the dense, avascular extracellular matrix (ECM) to reach their intended targets (e.g., chondrocytes). Small-molecule drugs such as glucocorticoid dexamethasone and matrix metalloproteinase (MMP) inhibitors, such as GM6001, are among those DMOAD candidates that could greatly benefit from targeted delivery in cartilage to reduce systemic side effects and increase efficacy by extending cartilage residence time, thereby lowering injection frequency and administration concentration.

There is a pressing unmet need in the market for novel compositions and methods for site-specific delivery of active agents to achieve desired outcomes, including ameliorating cartilage destruction and altering OA disease trajectory.

Opportunity

Dr. Marcolongo and her collaborators have developed innovative biomimetic proteoglycan (BPG) constructs that are designed to mimic natural proteoglycans in the body. These constructs are engineered to attach selected active agents, enabling precise delivery of sight-specific anti-inflammatory therapeutics. In preclinical studies, these constructs have demonstrated the ability to effectively diffuse across cellular membranes, facilitating direct and localized delivery of their therapeutic cargo to targeted sites of inflammation or injury.

Administration methods include injections, arthroscopic implantation, and open surgical implantation, providing flexibility in clinical application to meet different patient needs. *In vivo* preclinical testing in mice has revealed the Marcolongo carrier system can cross cellular membranes efficiently and BPGs remain within the joint cavity for up to 14 days, providing sustained therapeutic effect. Importantly, no detectable migration of fluorescently tagged agents was observed in vital organs such as the liver and kidneys, indicating a low risk of systemic spread and off-target effects.

This breakthrough addresses a significant challenge in current treatment modalities in mammals, where therapeutic agents often migrate away from the target site, reducing efficacy and increasing side effects. These BPG constructs represent a promising platform for the localized and sustained delivery of therapeutics, with potential applications in treating joint diseases and inflammatory conditions, offering improved safety and effectiveness.

[1] Siefen T, Bjerregaard S, Borglin C, Lamprecht A. Assessment of joint pharmacokinetics and consequences for the intraarticular delivery of biologics. J Control Release. 2022 Aug;348:745-759. doi: 10.1016/j.jconrel.2022.06.015. Epub 2022 Jun 25. PMID: 35714731.

Continued on back

Unique Attributes

- Preclinical *in vivo* tests indicate the BPGs are retained within the intended therapeutic area with no visible indication of migration of the therapeutic cargo away from the target site.
- Constructs have anti-catabolic or pro-anabolic chondrocyte metabolism, inhibit MMP activity, and inhibit aggrecanase activity.
- Constructs can engineer the immediate microniche of resident cells, thereby modulating and enhancing cell anabolic responses to external mechanical and biophysical stimuli

Commercial Applications

Designed to deliver therapeutic anti-inflammatory treatments for arthritis in a bovine live explant model, with minimal side effects. Additional benefits include

- Injectable to the knee intra-articular joint space,
- Molecular migration from joint space through cartilage thickness with delivery and repair to cartilage,
- Reduced amount of drug administration,
- Prolonged *in situ* release,
- Increased drug effectiveness compared to drug alone,
- Reduced cartilage degeneration, and
- Better preserved mechanical functions of cartilage.

Additional use cases include the delivery of cosmetical agents for dermatological issues to improve skin appearance, and repair dermatological problems such as scarring, burns, and sun damage. Other use cases include supplementation of heart valves for transplant, molecular engineering of the intervertebral disc.

Stage of Development

TRL 4: Technology Validated in the Lab

Intellectual Property

PCT application published as WO 2025/049740 A1, March 2025.

Licensing and Collaboration Opportunity

Villanova University is seeking a licensee for commercialization or an industry sponsor to support the further development of preclinical and clinical technologies.

INSTITUTIONAL CONTACT

Amanda M. Grannas, Ph.D.
VP & Chief Research Officer
+1 610.519.4881
Email

L2C PARTNERS CONTACT

Merle Gilmore, MBA
+1 610.662.0940
Email

Alex Toglia, MS
+1 610.937.1067
Email